Synthesis and Biomedical Applications of Medicinal Plant-Mediated Transition Metal Oxide Nanoparticles

A

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BY

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PROPOSAL FOR TOPIC APPROVAL TO BE SUBMITTED TO THE UNIVERSITY OF MUMBAI FOR THE Ph.D. DEGREE IN THE SUBJECT OF **CHEMISTRY**

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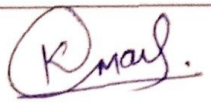
Signature of the Research Supervisor/Guide	:	

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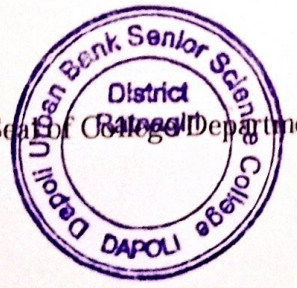

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1. TITLE: Synthesis and Biomedical Applications of Medicinal Plant-Mediated Transition Metal Oxide Nanoparticles

2. AIMS AND OBJECTIVES:

1. To identify and collect medicinal plants.
2. To authenticate the medicinal plant species from the Botanical Survey of India (B.S.I.), Pune.
3. To carried out phytochemical analysis of plant extract.
4. To synthesize Transition metal oxide nanoparticles (TMONPs) using medicinal plant extract as a capping/reducing/stabilizing agent.
5. Characterization of synthesized TMONPs by several analytical techniques such as XRD, UV-Visible, FT-IR, SEM-EDAX, HRTEM, XPS, VSM.
6. To explore biomedical applications with special emphasis on antidiabetic and anticancer properties.

3. INTRODUCTION:

In many developing countries around the world, plants are the richest source of medicines for humans as primary treatments from normal to life-threatening diseases. Traditional Chinese Medicine and Indian Ayurveda, the two well-known and old living traditions have contributed significantly to imparting many therapeutically important formulations. The World Health Organization (WHO) have declared a list of 21,000 medicinal plants which are utilized for medical purpose across the world. In India alone, 2500 plants have been investigated. Being the largest medicinal plant producer country, India is known as the 'botanical garden of the world' [1]. The Konkan region falls in the western Ghat region and has been declared a world heritage centre by UNESCO. So, many unique medicinal plants exist in this region.

In ancient times, the local medicine practitioners used to cure diseases by offering Bhasma or Churna, made in metal utensils. This was the indirect concept of preparing plant-based nanoparticles. They were using particular metals for preparing particular Churna or Bhasma. This concept could have led the foundation to develop a synthetic strategy for plant-mediated metal oxide nanoparticles [2].

Nanotechnology is a relatively new branch of science that has a wide range of applications from the production of energy to industrial production processes. The nanoparticles are the materials having a size below 100 nm i.e., 1 to 100 nm. An important feature of nanomaterials is their large surface area with minute

size[3]. The d-block metals, commonly known as transition metals, retain incomplete 'd' orbital due to which they differ from the rest of the metals. The incomplete 'd' orbital configuration is a fascinating property of these elements as it leads to multiple oxidation state enhancing their complex forming abilities. The transition metal oxide nanoparticles (TMONPs) can be engineered to possess unique compositions and functionalities. Recently, the synthesis of TMONPs using green methods garnered special attention due to their less environmental impact. The major advantage of green metal oxide nanoparticle synthesis is their availability at ease, safer, non-toxic, and non-harmful nature. The plant extract consists of a broad type of metabolites that can aid in the reduction of metal ions and are faster than microbes in biosynthesis. The synthesis of TMONPs by a green and inexpensive method with its biomedical application is a subject of current work[4-6]. Various transition metal oxide nanoparticles like gold, silver, platinum, zinc, copper, titanium, magnetic iron-ore, and nickel were synthesized from natural resources and are studied exclusively. The variety of applications for transition metal oxide nanoparticles is growing rapidly including electronic sensors, drug delivery, sensor, biological catalyst [7], domestic wastewater treatment, and photodegradation [8]. The biomedical applications of TMONPs is an emerging field of research.

A few TMONPs like iron oxide (Fe_2O_3), titanium oxide (TiO_2), and zinc oxide (ZnO), Copper oxide (CuO) have been explored. It is necessary to have the following properties for exhibiting the best biomedical applications: 1. Biocompatible 2. Chemically stable 3. Non-toxic 4. Resistance to wear and scratch. Most of the TMONPs possess some or all of the four properties. Further, MONPs with a size less than 20 nm have the ability to enter cell membrane, internal organelles, and can cross the blood-brain barrier. Superparamagnetic iron oxide nanoparticles (SPIONPs) are extensively used materials for drug delivery, imaging, and therapy against hyperthermia. Ferumoxytol (a form of Fe_3O_4 NPs) is used as an iron supplement and is approved by FDA. Some other iron oxide nanoparticles (FeNPs) have been utilized in preclinical and clinical agents for MRI. Being listed as a safe material, ZnO nanoparticles (ZnONPs) exhibit good antibacterial agents. It is also being utilized in the regeneration and repair of bones. *In-vitro* and *in-vivo* studies of titanium oxide nanoparticles (TiO_2NPs) exemplified their non-toxic nature. TiO_2NPs have been reported to possess promising antifungal, antibacterial, and anticancer activities. Curcumin decoration on TiO_2NPs was reported for effective wound healing. As copper oxide nanoparticles (CuONPs) possess some unique characteristics features like

good electrochemical potential, appropriate redox potential, and excellent stability in solutions, it has been employed for many more applications. The CuONPs have shown potential pharmacological activities, importantly in antitumor therapy. Being an excellent antibacterial agent, CuONPs have been utilized in wound dressing bandages and antimicrobial ointments. Moreover, their antimicrobial activities against various microbes like *E. coli*, *S. aureus*, *P. aeruginosa*, etc., are well known [9-14].

Traditionally most of the metal and metal oxide nanoparticles were routinely synthesized by various physical and chemical methods. Some of the commonly used synthetic methods are non-sputtering, co-precipitation, hydrothermal, sol-gel techniques, and electrochemical techniques. But the downside of these methods is that they require costly, toxic, and potentially hazardous, not to mention the difficult separation procedure, high pressure, and energy requirement. By using medicinal plant extracts, nanoparticle synthesis is advantageous when compared with chemical and physical methods. Because it is a cheaper and faster method involving only a single step, no side product or by-product form, it is eco-friendly, and it does not require high pressure, energy, or temperature.

4. PURPOSE OF THE STUDY:

Owing to a relatively newer method than orthodox methods of nanoparticle synthesis, the proposed study leads to non-hazardous, eco-friendly, and following the green chemistry ethics for the synthesis of novel transition metal oxide nanoparticles[15–18]. Further, the resulting nanoparticles will be tested for various biomedical applications (in-vitro, in-vivo).

5. STUDY BACKGROUND (LITERATURE REVIEW)

NATIONAL STATUS

i. Mukul Barwant and co-workers synthesized Ag/AgO/Ag_2O nanoparticles using *Solanum eleaegnifolium* leaves extract. In this study, they investigated selective pharmacological applications including antioxidant, anticancer, and DNA cleavage studies [19].

ii. Jyoti Dhatwalia and others synthesized Cu_2ONPs using fruit extract of *Rubus ellipticus*. They verified anticancer, antioxidant, and toxicological studies of synthesized metal oxide nanoparticles [20].

iii. G. Satishkumar and mates synthesized ZnONPs using *Couroupita guianesis Aubl.* leaves extract. They have reported the bactericidal effect of synthesized nanoparticles against human pathogens [21].

iv. Shreyas Pansambal and others synthesized fluorescent CuONPs using *Acanthospermum hispidium* L. leaves extract to verify antimalarial, antimycobacterial, and antimicrobial activities [22].

v. Suresh Ghotekar and co-workers synthesized silver nanoparticles for antimycobacterial, antibacterial, and antimalarial activities using *Leucaena leucocephala* L. leaves [23].

vi. N. Bhuvan Raj and others synthesized ZnONPs using *Syzygium cumini* plant extract for antimicrobial and photocatalytic activities. The best antimicrobial activity was reported against *P. aeruginosa* while the Acid red 88 dye was degraded efficiently [24].

INTERNATIONAL STATUS

i. H C Ananda Murthy and co-workers synthesized green copper nanoparticles using the Ethiopian medicinal plant *Hagenia abyssinica (Brace) JF. Gmel.* leaves extract. In this study, they investigated the effect of synthesized nanoparticles on selected bacterial pathogens [25]. This study concluded that the synergistic effect of bioactive components from medicinal plant attached to copper nanoparticles proved to enhance bioactivity.

ii. Muhammad Hafeez and mates synthesized cobalt oxide nanoparticles using medicinal plant *Populous ciliata* plant leaves available at Muzaffarabad, Pakistan, and evaluated their bioactivities against some selected bacterial strains [26].

iii. Banzeer Abbasi and co-workers synthesized Ag_2O nanoparticles using aqueous and ethanolic leaves extract of *Rhamnus virgata* species. They utilized as-synthesized nanoparticles for anticancer, antimicrobial, antidiabetic, antiradical, biocompatibility, and protein kinase inhibition assay [27].

iv. Abel Saka and others synthesized TiO_2 nanoparticles using Papaya (Caricaceae) shell extract from Ethiopia and evaluated antifungal applications [28].

v. Shakeel Ahmad Khan and co-workers synthesized chromium oxide nanoparticles using *Abutilon indicum* (L.) as a capping agent. The

antibacterial, anticancer, and antioxidant activities were evaluated against synthesized nanomaterial [29].

vi. Sareh Ghorbani and others synthesized manganese oxide (MnO_2) using cumin extract and were then composited with medicinal plant *Hypercom perforatum.* As prepared manganese oxide nanoparticles were tested for antimicrobial and anticancer activities [30].

6. RESEARCH HYPOTHESIS:

The detailed study of novel medicinal plant-mediated TMONPs will be helpful in various biomedical applications.

7. RATIONAL HYPOTHESIS:

The transition metal oxide nanoparticles possess effective biological, catalytic, magnetic, and photocatalytic properties. Therefore, they are employed in bioimaging, biosensing, supercapacitor, and photovoltaic applications. In particular, they can be used as drug carriers, drug delivery agents, as well as anticancer, antidiabetic, and antimicrobial agents along with ex-vivo live cell imaging.

8. RESEARCH METHODOLOGY (MATERIALS AND METHODS)

- Easily available, inexpensive, non-toxic, and preferably biodegradable precursors will be used.
- The transition metal oxide nanoparticles will be synthesized by using medicinal plant extract, metal salt solution, complexing reagent, etc.
- The AR-grade chemicals will be used for this work.

Synthesis of Metal Oxides

- The fresh parts of the medicinal plant will be collected and after thorough washing, the extract will be prepared.
- Phytochemical analysis of plant extract will be carried out to know presence of important biomolecules.
- The metal salt solution of different concentrations (1M, 0.1M, and 0.01M) will be prepared.
- The optimization study will be carried out by mixing different concentrations of plant extract and metal salt solution.
- After optimization, the fixed composition of metal salt and plant extract will be mixed to get desired TMONPs.

- Special emphasis will be given to getting TMONPs of reduced size, possibly below 10nm by maintaining various parameters like temperature, pH, concentration, etc.
- The nanoparticles will then be centrifuged and dried at a desired temperature in a muffle furnace.
- The dried material will be collected, stored and used for further work.

Characterization of Synthesized Nanoparticles

- The obtained nanoparticle will be characterized by different analytical techniques viz. UV-Visible Spectrometer, X-Ray diffractometer (XRD), transmission electron microscopy (TEM), scanning electron microscopy (SEM), Energy Dispersive X-ray spectral analysis (EDS), X-ray photoelectron spectroscopy (XPS) & Vibrating sample magnetometer (VSM).

Biomedical applications of synthesized nanoparticles

- The synthesized nanoparticles will be tested for various biomedical applications including in-vitro, in-vivo antimicrobial, antidiabetic, and anticancer activities.

9. EXPECTED OUTCOMES:

- The successful completion of work will result in the advancement of a newer synthetic route of transition metal oxide nanoparticles to overcome the synthetic difficulties arising from conventional methods.
- The resultant cost-effective, green metal oxide nanoparticles will possess improved biomedical properties.
- Based on the experimental outcome, several research papers with scientific value and dissemination to chemistry and material science conference/publications are planned.

10. LIMITATION OF THE STUDY

Though we will be using inexpensive easily available, nontoxic, and biodegradable raw materials. So some apprehensions need to be addressed.

- By controlling parameters like temperature, size, shape, etc. we can accurately/preciously control process.

11. STATISTICAL PLAN (THREE YEAR):

Months	Plan of Research Work
1 to 6	Coursework Completion and Literature Review
7 to 14	Laboratory Work
15 to 24	Result analysis and Research paper publication
25 to 36	Synopsis and Thesis Writing

12. RESEARCH DESIGN:

Phase I: Identification, Collection, and authentication of medicinal plants and Review of the literature.

Phase II: Medicinal plant-mediated synthesis of transition metal oxide nanoparticles.

Phase III: Characterization of transition metal oxide nanoparticles.

Phase IV: Biomedical evaluation of transition metal oxide nanoparticles.

Phase V: Preparation and publication of Research papers in UGC Care listed /Scopus Indexed/SCI indexed journals.

Phase VI: Write up and submission of Thesis.

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